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U. S. Naval School of Aviation Medicine

U. S. NAVAL AIR STATION
PENSACOLA, FLORIDA

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RESEARCH REPORT

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SUMMARY

The purpose of this study was to determine concentrations of carbon monoxide in air required to give a carboxyhemoglobin increase of 7% in subjects at rest at an altitude of 10,000 feet. Exposure times of 5, 3, and 1 minute(s) and 40, 20, and 10 seconds were used. The concentrations of carbon monoxide required were 0.55, 0.975, 2.63, 3.28, 5.70, and 18.35%, respectively. When adjusted to standard conditions, these figures fit the curve derived from Pace's formula (1):

$$\Delta \% \text{ COHb} = \frac{\text{Parts CO} \times \text{MinVol} \times \text{Exposure Time}}{42.5 \times \text{Blood volume}}$$

INTRODUCTION

A method for predicting carbon monoxide uptake by man has been developed by Pace (1) using as parameters the concentration of carbon monoxide, altitude, and exposure time. His nomogram does not extend to a period of less than one minute, and when using an increase of carboxyhemoglobin of 7% as the end point, the nomogram does not extend below a period of 20 minutes. The purpose of this study was to extend the observations of Pace using exposure times of 5, 3, 1 minute(s) and 40, 20, and 10 seconds. Determinations were made of the concentrations of carbon monoxide in air required to give a carboxyhemoglobin increase of 7% (2) in human subjects, at rest, at a simulated pressure altitude of 10,000 feet, and a temperature of +70° F.

EXPERIMENTAL PROCEDURE

A. Subjects

Five Navy Hospitalman volunteers were given appropriate physical and psychological examinations. Control respiratory patterns (MRV, cycles/minute, rate of inspiration/expiration, etc.), blood volumes (3), hematocrits, and hemoglobin determinations were made, and each man's age, weight, and height was noted (Table 1).

All subjects were smokers; no attempt was made to control smoking before subjects entered the chamber.

B. Apparatus

A low pressure chamber was used to simulate a pressure altitude of 10,000 feet. An aircraft altimeter, calibrated by mercury manometer, was used to control the altitude with an accuracy of ±40 feet (0.8mmHg). Temperature was maintained in the chamber at +70° F (±1½°).

During the test, subjects breathed known concentrations of carbon monoxide in air from a Collins 120 liter spirometer through an A13A oxygen mask (Plate 1). The spirometer was contained within the low pressure chamber and the gas was delivered to the subject at that barometric pressure. The oxygen mask was checked for leak and fit and the hose was flushed with the gas mixture up to the mask inhalation valves before each exposure.

The kymograph on the Collins spirometer was modified so that wax-coated paper could be used to record respiratory data. The rate of rotation of the drum was increased to one revolution per minute; in this way respiratory minute volume (Table 2), rate and depth of inspiration, total quantity of gas used, and number of respiratory cycles could be obtained during the test exposures.

Control respiration studies were made with a Sanborn Waterless Metabolism tester modified so that the kymograph rate of rotation was one revolution per minute. Control determinations were made at sea level, +20°C, with subjects breathing oxygen.

C. Techniques

Each subject was given a 30 minute pre-exposure period at 10,000 foot pressure to allow him to become quiet, rested, and psychologically adapted to his environment. Blood gas changes tend to be stabilized to the 10,000 foot pressure in that time. Immediately before exposure to the carbon monoxide-air mixture, a 5 cc blood sample was taken from the antecubital vein; the 19 gauge modified lumbar puncture needle was allowed to remain indwelling (Plate 1). A stilette was inserted in the needle to prevent clotting or escape of blood. The subject remained at 10,000 feet an additional five-minute period after exposure to the carbon monoxide-air mixture before the post-exposure blood sample was taken. The increase in carboxyhemoglobin expressed in % (pre-exposure carboxyhemoglobin % subtracted from post-exposure carboxyhemoglobin %) has been expressed by Pace (1) as Δ %COHb and this terminology will be used in this report.

Two Δ %COHb determinations were made for each subject and time interval. If the calculated carbon monoxide mixture gave a Δ %COHb of less than 7, on the second exposure, at the same time interval, the subject was given a higher percentage of carbon monoxide in an attempt to produce a Δ %COHb equal to or slightly greater than 7. Extrapolation or interpolation was used to determine the percentage of carbon monoxide expected to give a Δ %COHb of 7.

On all 20- and 10-second exposures, timing was started at the beginning of an inhalation. This was especially important in the 10-second exposure since an average of only three inhalations (minimum two, maximum four) occurred during this interval.

A minimum of 48 hours was allowed between exposures for any one subject.

All carboxyhemoglobin determinations were made using the Van Slyke technique (4). Total hemoglobin determination was made on each pre-exposure blood sample by the cyanmethemoglobin method (5). All calculations were based on the fact that the oxygen combining capacity of the blood is equal to the grams percent hemoglobin divided by 0.736, disregarding minor corrections due to methemoglobin and inactive hemoglobin. Necessary corrections were made for individual hemoglobins.

Hematocrits were determined by the Wintrobe method (6).

RESULTS AND DISCUSSION

Results are summarized in Figures 1-3 and Tables 1 and 2.

Pace's nomogram (1) does not extend to a period of less than 20 minutes when using a Δ %COHb of 7 as the end point. His formula* was used to approximate percentage of carbon monoxide required to give a Δ %COHb of 7, but in nearly all determinations the actual Δ %COHb was less than the calculated, due in part to our subjects' lower minute respiratory volume (MRV). Since MRV could not be anticipated, a second determination with a higher concentration of CO at the same time interval was necessary in every case. The two Δ %COHb determinations were plotted and the points joined with a straight line (8). Interpolation or extrapolation was used to determine the amount of carbon monoxide expected to give a Δ %COHb of 7.

Pace's data for CO required to give a Δ %COHb of 7, and our data, as determined by the above procedure, are plotted in Figure 3. It may be seen that our values differ considerably from those given by Pace's formula when his average values for blood volume and MRV are used. If, on the other hand, the values for blood volume and MRV as determined in this study are substituted in Pace's formula, there is excellent correspondence between our data and those predicted by Pace's formula (Fig. 3). The deviations of the latter two curves from Pace's original curve are attributable to higher average blood volumes and lower average MRV's in our subjects. The discrepancy is particularly marked at 10-second exposure times, when the average MRV for our subjects was 8.1 liters per minute, body temperature and pressure, saturated (lpm, BTPS).

The findings reported in this study may be applied to specific situations in which aerial gunners are exposed to high concentration - short time contamination of carbon monoxide. However, average respiratory minute volume for the five test subjects reported in this study was 11.52 lpm, BTPS. It has been reported (7) that a crewman gunner firing a free 50 caliber waist gun-camera under simulated combat conditions for 23 minutes out of a 30 minute test period ventilated a maximum of 40.7 lpm BTPS, with an average of 20.6 lpm BTPS for all gunners at 20, 25, and 30,000 feet. Studies at Pensacola reported a maximum of 20.8 lpm (37°C. ambient, at sea level) (9). These reports would indicate that an allowance must be made for probably increased ventilation rate due to exercise found in gunners since it has been stated by various authors (8) that CO uptake varies with the activity of the subject.

Factors affecting uptake of CO are (8) partial pressure CO of inspired air, partial pressure oxygen of inspired air, total ambient pressure, partial pressure CO and percent COHb existing at zero time, duration of exposure, alveolar ventilation,

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$$* \quad \Delta\%\text{COHb} = \frac{\text{Parts CO X Min. Vol. X Exposure Time}}{\text{42.5 X Blood Vol.}}$$

circulation through the lung, duration of exposure of blood to alveolar air and instantaneous amount of blood in the alveolar bed, hemoglobin and perhaps myoglobin mass, and the kinetics of the combinations and dissociations between CO, O_2, and Hb.

Some subjects showed a decreased Δ %COHb with the increased carbon monoxide concentration at the same time interval (Fig. 1, A and B). These irregularities are the result of decreased ventilation or other physiological variations.

An additional subject (C.A.P.) inhaled 500 cc of 100 percent CO in $2\frac{1}{2}$ seconds at sea level altitude, with a Δ %COHb of 13.7 percent, indicating that 194 cc of CO was absorbed. The subject was under the impression that less than 500 cc of gas had been inhaled. Possibly the 194 cc diffused across the alveolar membrane so rapidly that the entire 500 cc was not in the lungs at any time. Of the 500 cc of CO inhaled, approximately 150 cc was in the dead air spaces (mouth, trachea, bronchi, etc.). Of 350 cc of alveolar CO, 194 cc, or 55 percent, was combined with hemoglobin as the result of a single $2\frac{1}{2}$-second inhalation. The only subjective symptom was a transient dizziness.

The same subject inhaled 500 cc of 50% carbon monoxide in air under test conditions (10,000 feet and +70°F) in 2 seconds, with a Δ %COHb of 8.9. Of 250 cc of CO in the gas mixture, 75 cc was in the "dead air" spaces. Only 175 cc of gas was available in the alveoli, but the subject absorbed an equivalent of 185 cc (126 cc at sea level). This discrepancy could be the result of experimental error, that some CO was absorbed in the dead air spaces, or that there was a mechanical flow of carbon monoxide from the dead air spaces to the alveoli due to reduced pressure caused by the rapid absorption of carbon monoxide in the alveoli. The subject again experienced the sensation that less than 500 cc of gas was inhaled. No subjective symptoms were noted.

It might be of interest to study, under closely controlled conditions, the uptake of high concentrations of carbon monoxide (25-100%) for short periods of time (20-2 seconds).

CONCLUSIONS

1. Relatively high concentrations of carbon monoxide in air can be tolerated by man for short periods of time.

2. The formula for estimating Δ%COHb developed by Pace (1) applies in this study of short exposure times.

Appreciation is gratefully extended to Jorma I. Niven, Ph. D. and Dietrich E. Beischer, Ph. D., who acted as consultants for this study.

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TABLE I

Control Data on Test Subjects

Determination	Ei 1	Ka 2	Ma 3	Mc 4	St 5
1. Age	31	19	21	20	25
2. Wt.	152.5	184	160	146	156
3. Ht. (inches)	69.75	77	67	68.50	72.50
4. Body area (sq.meters)	1.82	2.1	1.78	1.76	1.85
5. Blood volume (liters)	6.01	6.93	5.87	5.81	6.10
6. Hematocrit	51.5	47.8	44.9	50.4	44.2
7. Hemoglobin	17.0	16.3	15.1	16.3	15.6
8. Normal Resp.					
a. MRV 1/m	7.096	9.52	9.52	9.5	12.695
b. Tidal air (cc)	546	952	952	791	746
c. Respiration (cycles/min)	13	10	10	12	17
d. Holds inspiration in secs.	0.33	0.498	0.57	0.32	0.40
e. Holds expiration in secs.	0.44	0.754	0.57	0.49	0.62
9. BMR	-4%	-24%	-17%	-12%	-20%

TABLE 2

Physiologic Data Obtained Under Test Conditions of 10,000 Feet Pressure Altitude, +70°F, Subjects at Rest

Determinations	Subjects #1 Ei	#2 Ka	#3 Ma	#4 Mc	#5 St
Time intervals	3 min.	3 min.	3 min.	3 min.	3 min.
A. Low concentration					
1. % CO	0.7%	0.7%	0.7%	0.7%	0.7%
2. Pre-exposure %COHb	4.4%	2.1%	3.1%	5.0%	2.0%
3. Δ% COHb	3.1%	7.1%	5.8%	6.4%	5.5%
4. Number of inhalations					
5. MRV 1/m BTPS	8.92	10.26	12.086	11.77	9.589
B. High concentration					
1. % CO	0.8%	0.8%	0.8%	0.8%	0.8%
2. Pre-exposure % COHb	3.4%	3.5%	3.1%	8.9%	2.4%
3. Δ% COHb	4.0%	7.8%	5.8%	7.5%	5.3%
4. Number of inhalations					
5. MRV, 1/m BTPS	6.42	16.56	9.098	13.64	10.83
Time intervals	1 min.	1 min.	1 min.	1 min.	1 min.
A. Low concentration					
1. % CO	1.0%	1.0%	1.0%	1.0%	1.0%
2. Pre-exposure % COHb	3.8%	3.6%	2.5%	5.4%	2.8%
3. Δ% COHb	2.5%	4.0%	2.6%	2.5%	2.9%
4. Number of inhalations	13	10	10	12	17
5. MRV, 1/M BTPS	9.63	22.077	16.59	14.45	10.055
B. High concentration					
1. % CO	1.5%	1.5%	1.5%	1.5%	1.5%
2. Pre-exposure % COHb	4.5%	5.0%	2.1%	5.0%	2.5%
3. Δ% COHb	3.3%	5.5%	3.7%	5.9%	2.4%
4. Number of inhalations	14				
5. MRV 1/M BTPS	10.43	16.725	8.83	15.119	10.436
Time intervals	40 sec.	40 sec.	40 sec.	40 sec.	40 sec.
A. Low concentration					
1. % CO	2.5%	2.5%	2.5%	2.5%	2.5%
2. Pre-exposure % COHb	4.1%	2.7%	2.7%	3.9%	2.8%
3. Δ% COHb	2.8%	3.9%	6.2%	5.0%	5.9%
4. Number of inhalations	12	8	14	7	18
5. MRV 1/m BTPS	7.79	10.41	13.62	8.39	13.36

Table 2 (Continued)

Determinations	Subjects #1	#2	#3	#4	#5
Time intervals	40 sec.	40 sec.	40 sec.	40 sec.	40 sec.
B. High concentration					
1. % CO	3.6%	3.6%	3.6%	3.7%	3.6%
2. Pre-exposure % COHb	3.8%	3.5%	3.0%	3.7%	2.2%
3. Δ% COHb	6.2%	7.4%	12.8%	9.1%	4.3%
4. Number of inhalations	12	8	15	9	15
5. MRV 1/m BTPS	7.39	10.83	14.185	13.28	12.467
Time intervals	20 sec.	20 sec.	20 sec.	20 sec.	20 sec.
A. Low concentration					
1. % CO	3.6%	3.85%	3.7%	3.85%	3.85%
2. Pre-exposure % COHb	3.8%	3.5%	2.3%	5.5%	3.4%
3. Δ% COHb	2.7%	5.6%	3.9%	6.1%	3.3%
4. Number of inhalations	6	4	5	5	7
5. MRV 1/m BTPS	9.99	13.186	13.18	16.78	11.988
B. High concentration					
1. % CO	5.0%	5.0%	5.0%	5.0%	5.0%
2. Pre-exposure % COHb	4.9%	6.0%	3.7%	5.1%	3.7%
3. Δ% COHb	4.0%	4.7%	10.3%	6.5%	4.9%
4. Number of inhalations	5	5	6	4	7
5. MRV 1/m BTPS	7.99	11.35	20.379	14.555	12.387
Time intervals	10 sec.	10 sec.	10 sec.	10 sec.	10 sec.
A. Low concentration					
1. % CO		7.5%	5.0%	9.6%	9.6%
2. Pre-exposure % COHb		4.6%	3.9%	5.4%	3.4%
3. Δ% COHb		3.3%	0.9%	5.6%	3.9%
4. Number of inhalations		2	3	2	3
5. MRV 1/m BTPS		9.99	7.19	9.99	9.19
B. High Concentration					
1. % CO		12.9%	12.9%	12.9%	12.9%
2. Pre-exposure % COHb		4.5%	2.4%	3.2%	2.6%
3. Δ% COHb		5.3%	4.7%	4.2%	4.4%
4. Number of inhalations		2	3	3	3
5. MRV 1/m BTPS		9.59	7.11	7.15	4.555

Fig. 1 A Carbon Monoxide Required to Give Indicated Carboxyhemoglobin Increases Over Indicated Time Intervals.

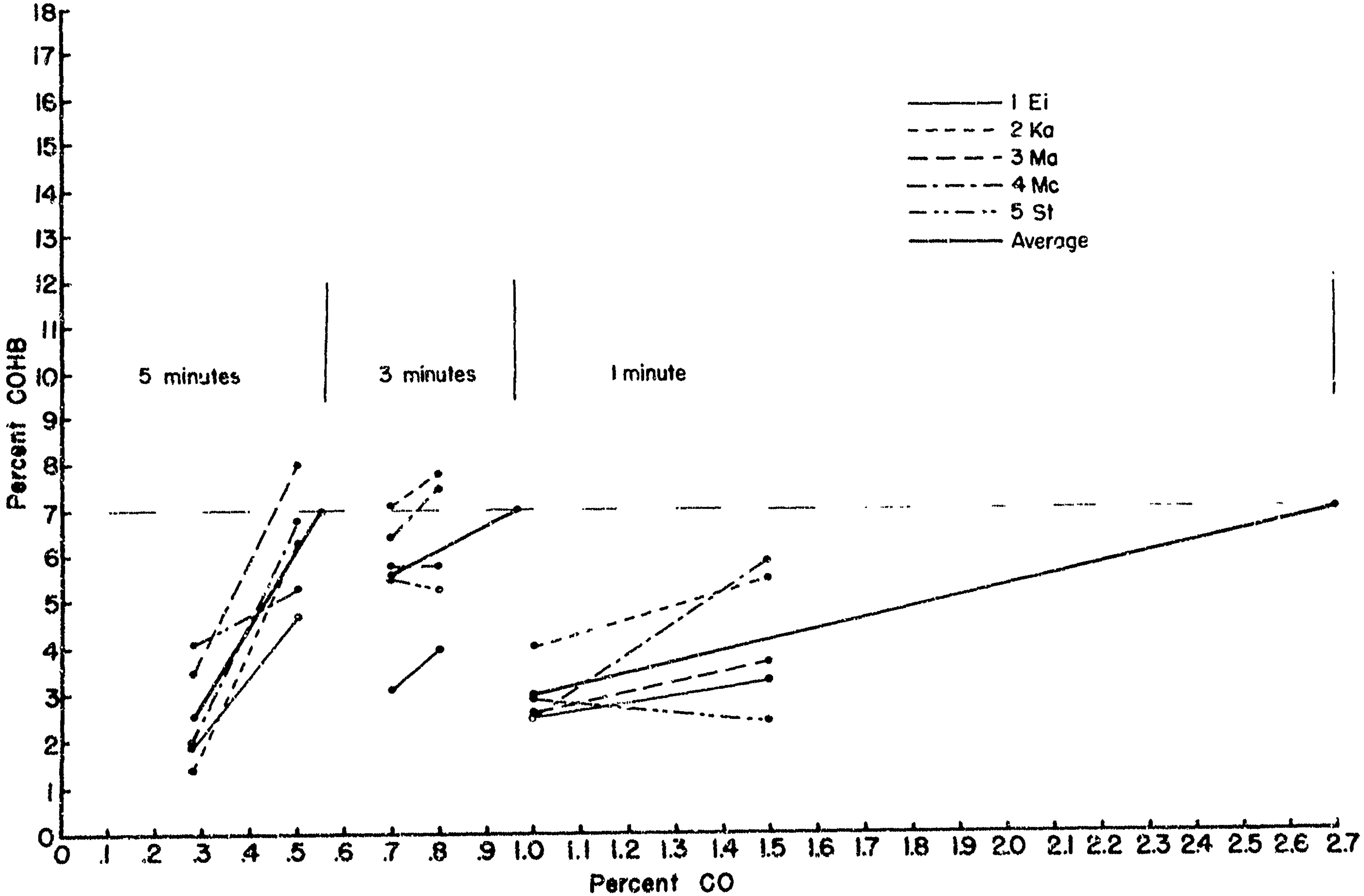
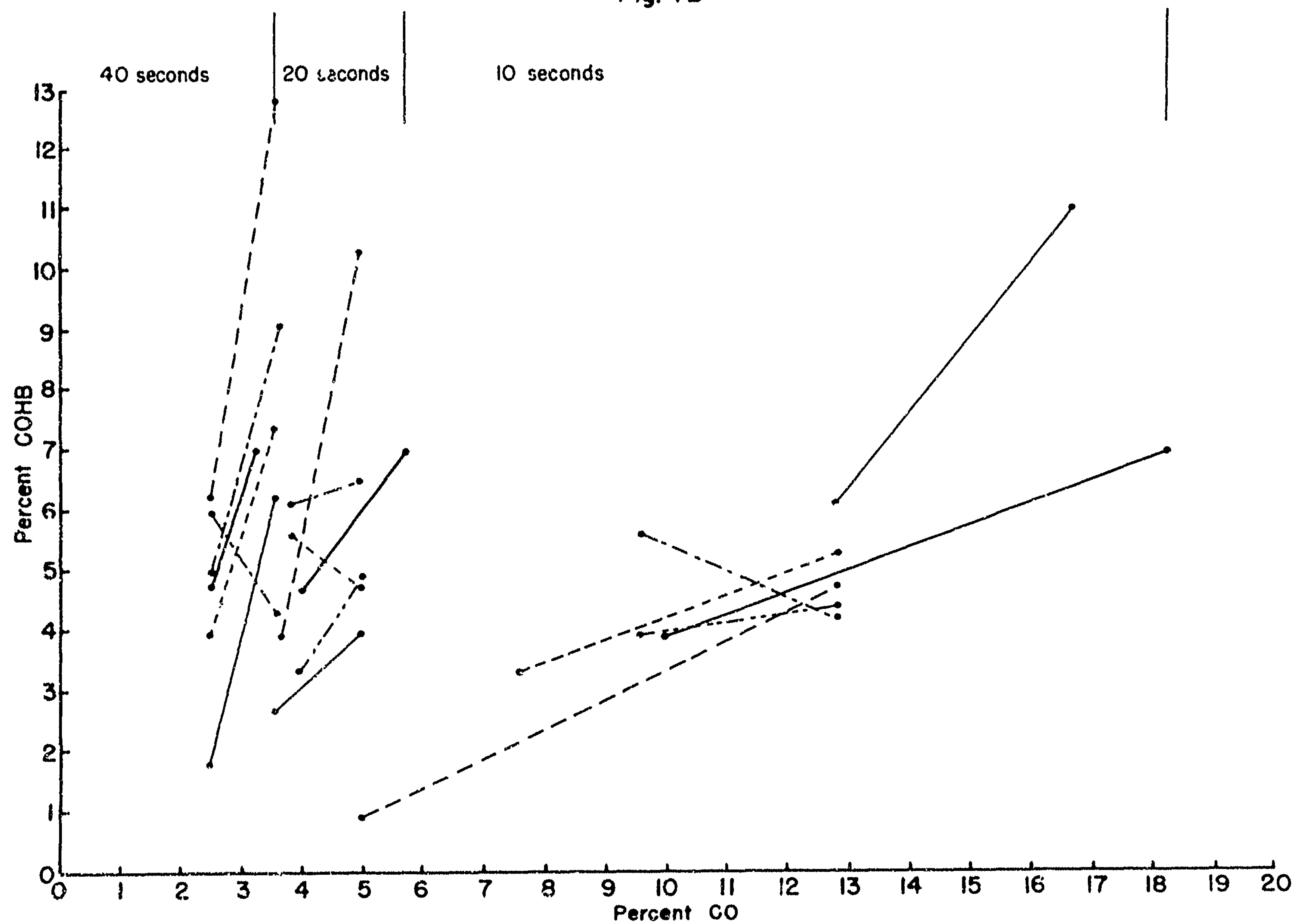


Fig. 1B


40 seconds
20 seconds
10 seconds
Percent COHB
Percent CO
0
1
2
3
4
5
6
7
8
9
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19
20

Fig. 2 Time-Carbon Monoxide Required to Give an Increase of Carboxyhemoglobin of 7%

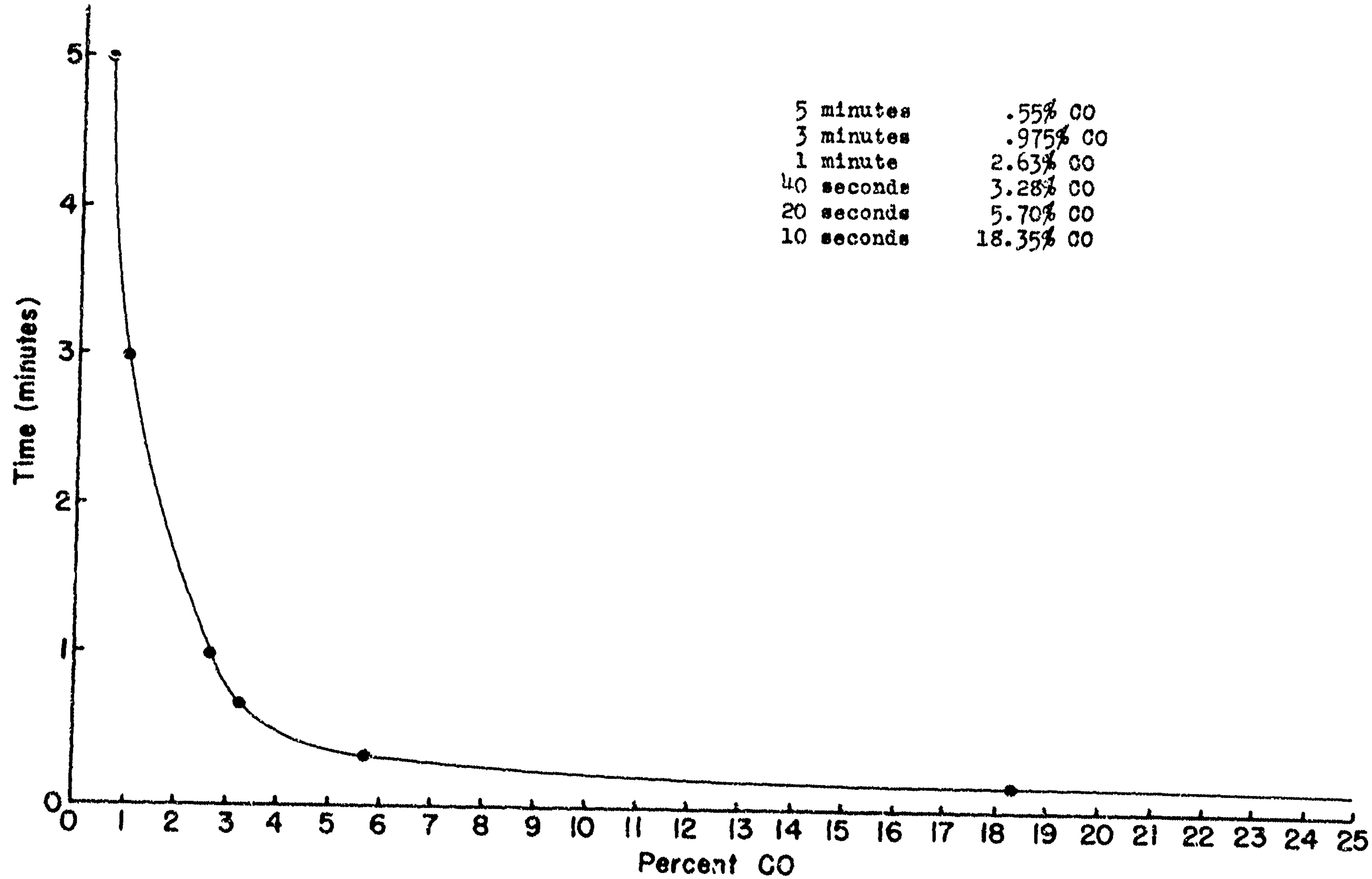
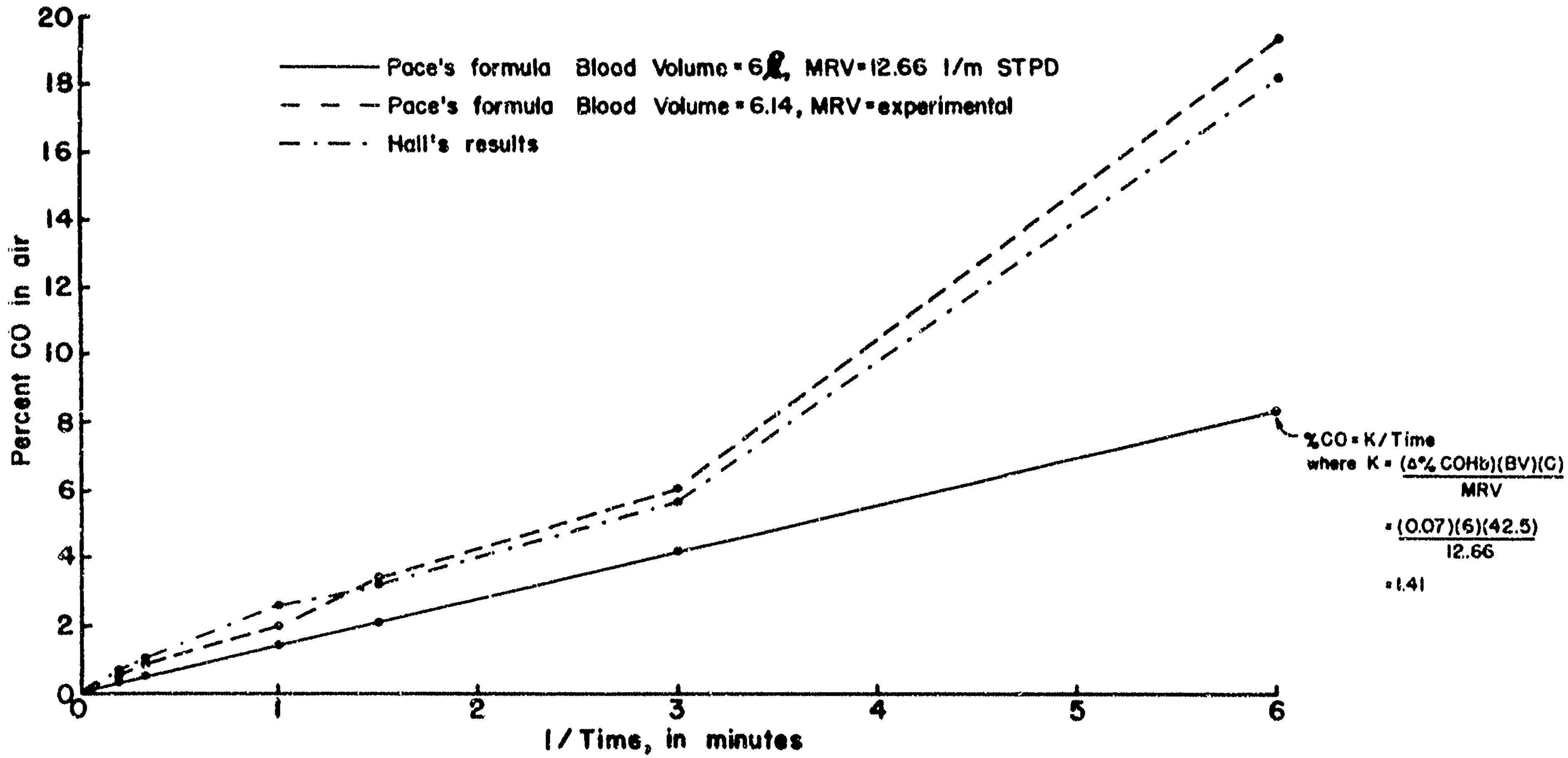
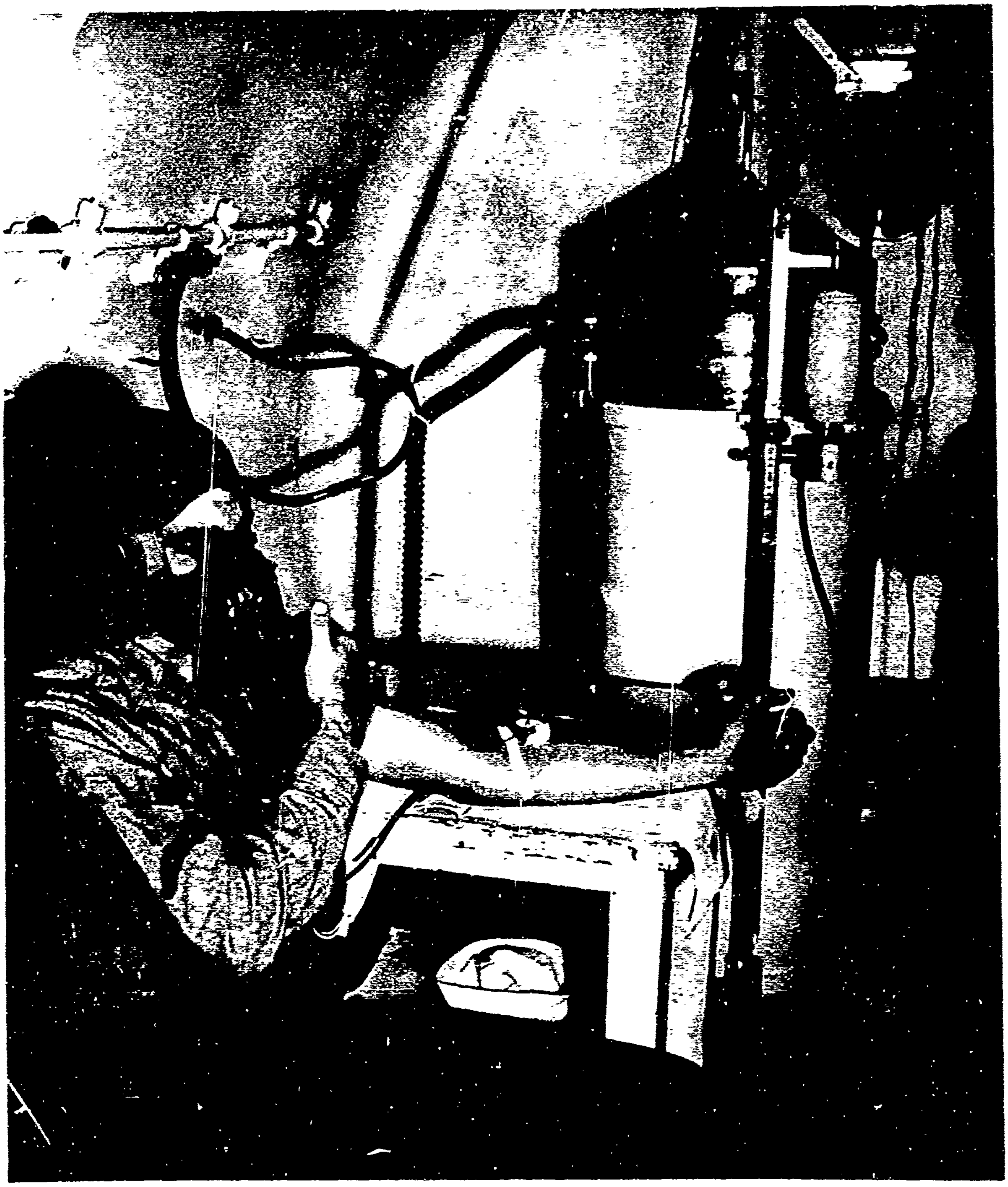


Fig. 3 Percent CO in Air Required to Give a Δ% COHb of 7 at Indicated Exposure Times





[redacted] Subject #4 breathing carbon monoxide and air at 10,000 feet simulated pressure altitude. Indwelling needle with stilette in place and spirometer with kymograph are shown.

PLATE I.